UROS gene

uroporphyrinogen III synthase

Normal Function

The *UROS* gene provides instructions for making an enzyme known as uroporphyrinogen III synthase. This enzyme is involved in the production of a molecule called heme. Heme is vital for all of the body's organs, although it is most abundant in the blood, bone marrow, and liver. Heme is an essential component of iron-containing proteins called hemoproteins, including hemoglobin (the protein that carries oxygen in the blood).

The production of heme is a multi-step process that requires eight different enzymes. Uroporphyrinogen III synthase is responsible for the fourth step in this process, in which hydroxymethylbilane (the product of the third step) is rearranged to form uroporphyrinogen III. In subsequent steps, four other enzymes produce and modify compounds that ultimately lead to heme.

Health Conditions Related to Genetic Changes

porphyria

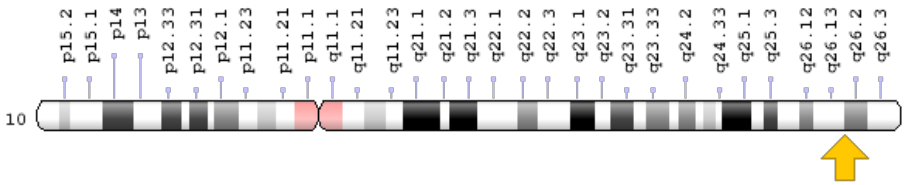
More than 35 mutations in the *UROS* gene have been found to cause a form of porphyria known as congenital erythropoietic porphyria. Most of these mutations change single protein building blocks (amino acids) in uroporphyrinogen III synthase. The most common *UROS* gene mutation, which is found in about one-third of all cases of congenital erythropoietic porphyria, replaces the amino acid cysteine with the amino acid arginine at position 73 (written as Cys73Arg or C73R). Several other mutations occur in a nearby region of DNA that regulates the activity of the *UROS* gene.

Mutations in or near the *UROS* gene alter the structure and function of uroporphyrinogen III synthase, which reduces the enzyme's activity. A shortage of functional uroporphyrinogen III synthase allows compounds called porphyrins to build up in developing red blood cells. These compounds are formed during the normal process of heme production, but reduced activity of uroporphyrinogen III synthase allows them to accumulate to toxic levels. The excess porphyrins can leak out of developing red blood cells and be transported through the bloodstream to the skin and other tissues. An accumulation of these substances in the skin causes oversensitivity to sunlight and the other characteristic features of congenital erythropoietic porphyria.

Chromosomal Location

Cytogenetic Location: 10q26.2, which is the long (q) arm of chromosome 10 at position 26.2

Molecular Location: base pairs 125,784,980 to 125,823,268 on chromosome 10 (Homo sapiens Annotation Release 108, GRCh38.p7) (NCBI)



Credit: Genome Decoration Page/NCBI

Other Names for This Gene

- Cosynthase
- HEM4_HUMAN
- Hydroxymethylbilane hydro-lyase (cyclizing)
- UROIIIS
- Uroporphyrinogen co-synthetase
- Uroporphyrinogen-III cosynthase
- Uroporphyrinogen III Cosynthetase
- Uroporphyrinogen-III Synthase
- uroporphyrinogen III synthase (congenital erythropoietic porphyria)
- Uroporphyrinogen III Synthetase
- Uroporphyrinogen Isomerase

Additional Information & Resources

Educational Resources

- Biochemistry (fifth edition, 2002): Mammalian Porphyrins Are Synthesized from Glycine and Succinyl Coenzyme A
  https://www.ncbi.nlm.nih.gov/books/NBK22446/#A3395

GeneReviews

- Congenital Erythropoietic Porphyria
  https://www.ncbi.nlm.nih.gov/books/NBK154652

Scientific Articles on PubMed

- PubMed
  https://www.ncbi.nlm.nih.gov/pubmed?term=%28%28UROS%5BTIAB%5D%29+OR+%28uroporphyrinogen+III+synthase%5BTIAB%5D%29%29+OR+%28%28UROIIIS%5BTIAB%5D%29+OR+%28Uroporphyrinogen+III+Cosynthetase%5BTIAB%5D%29+OR+%28Uroporphyrinogen+III+Synthetase%5BTIAB%5D%29+OR+%28Uroporphyrinogen+Isomerase%5BTIAB%5D%29+OR+%28Uroporphyrinogen-III+cosynthase%5BTIAB%5D%29+OR+%28Uroporphyrinogen-III+Synthase%5BTIAB%5D%29%29+AND+%28%28Genes%5BMH%5D%29+OR+%28Genetic+Phenomena%5BMH%5D%29%29+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+3240+days%22%5Bdp%5D

OMIM

- UROPORPHYRINOGEN III SYNTHASE
  http://omim.org/entry/606938

Research Resources

- ClinVar
  https://www.ncbi.nlm.nih.gov/clinvar?term=UROS%5Bgene%5D
- HGNC Gene Symbol Report
  http://www.genenames.org/cgi-bin/gene_symbol_report?q=data/hgnc_data.php&hgnc_id=12592
- NCBI Gene
  https://www.ncbi.nlm.nih.gov/gene/7390
- UniProt
  http://www.uniprot.org/uniprot/P10746

Sources for This Summary

- Badminton MN, Elder GH. Molecular mechanisms of dominant expression in porphyria. J Inherit Metab Dis. 2005;28(3):277-86. Review.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/15868463
- Desnick RJ, Astrin KH. Congenital erythropoietic porphyria: advances in pathogenesis and treatment. Br J Haematol. 2002 Jun;117(4):779-95. Review.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/12060112

- Elder GH. Genetic defects in the porphyrias: types and significance. Clin Dermatol. 1998 Mar-Apr; 16(2):225-33. Review.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/9554235
- Fortian A, Castaño D, Ortega G, Laín A, Pons M, Millet O. Uroporphyrinogen III synthase mutations related to congenital erythropoietic porphyria identify a key helix for protein stability. Biochemistry. 2009 Jan 20;48(2):454-61. doi: 10.1021/bi801731q.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/19099412
- Kauppinen R. Porphyrias. Lancet. 2005 Jan 15-21;365(9455):241-52. Review.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/15652607
- Sassa S, Kappas A. Molecular aspects of the inherited porphyrias. J Intern Med. 2000 Feb;247(2): 169-78. Review.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/10692079
- Schubert HL, Raux E, Matthews MA, Phillips JD, Wilson KS, Hill CP, Warren MJ. Structural diversity in metal ion chelation and the structure of uroporphyrinogen III synthase. Biochem Soc Trans. 2002 Aug;30(4):595-600. Review.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/12196144
- Shady AA, Colby BR, Cunha LF, Astrin KH, Bishop DF, Desnick RJ. Congenital erythropoietic porphyria: identification and expression of eight novel mutations in the uroporphyrinogen III synthase gene. Br J Haematol. 2002 Jun;117(4):980-7.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/12060141
- Solis C, Aizencang GI, Astrin KH, Bishop DF, Desnick RJ. Uroporphyrinogen III synthase erythroid promoter mutations in adjacent GATA1 and CP2 elements cause congenital erythropoietic porphyria. J Clin Invest. 2001 Mar;107(6):753-62.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/11254675
  Free article on PubMed Central: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC208941/
- To-Figueras J, Badenas C, Mascaró JM, Madrigal I, Merino A, Bastida P, Lecha M, Herrero C. Study of the genotype-phenotype relationship in four cases of congenital erythropoietic porphyria. Blood Cells Mol Dis. 2007 May-Jun;38(3):242-6. Epub 2007 Jan 31.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/17270473

Reprinted from Genetics Home Reference:
https://ghr.nlm.nih.gov/gene/UROS

Reviewed: July 2009
Published: March 21, 2017

Lister Hill National Center for Biomedical Communications
U.S. National Library of Medicine
National Institutes of Health
Department of Health & Human Services